REMARKS

Applicants appreciate the further confirmation of allowable subject matter, i.e. that claims 91-102 and 143 are allowed.

The undersigned also thanks Primary Examiner Helms for his time and for his helpful comments during their discussion of the present application on April 5, 2005.

Claims 122 and 142 have been canceled without prejudice.

Claims 123, 132-139 were rejected under 35 U.S.C. § 102(b) over Buday, et al., *The Journal of Biological Chemistry* 269: 9019-9023, 1994 (Buday).

Claims 123-131 were similarly rejected under 35 U.S.C. § 102(e) over Hirth, et al., U.S. Patent 5,058,959 (Hirth).

For the sake of brevity, these two Section 102 rejections are addressed in combination.

As the rejections are understood, in accordance with the recent discussions with Primary Examiner Helms, the position is taken that, in the absence of evidence to the contrary, it may be *possible* the antibodies reported in Buday et al. and Hirth et al. could "specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4."

Primary Examiner Helms also related to the undersigned that submitting evidence of record that would tend to rebut such postulated possibility could provide a basis for withdrawal of the rejections.

Each of the rejections is traversed.

The anti-phosphotyrosine antibody disclosed by Buday is the 4G10 antibody sold by Upstate (A certificate of analysis of the 4G10 antibody is attached hereto as Exhibit A.) Hirth does not disclose which anti-phosphotyrosine antibody was used but only that an anti-phosphotyrosine serum was used (Col. 25, lines 26-27).

It is well known that anti-phosphotyrosine antibodies do not bind to every phosphorylated tyrosine of every protein. That is, it is well known that anti-phosphotyrosine antibodies have specificity and selectivity. Thus, for instance, attached as Exhibits A and B are copies of certificates of analysis of two different anti-phosphotyrosine antibodies sold by Upstate, the cited 4G10 antibody and a rabbit polyclonal anti-phosphotyrosine antibody mixture. These certificates of analysis show that under the same conditions, different proteins were recognized by the different antibodies. In turn, these certificates of anyalsis show that not every tyrosine phosphorylated antibody will recognize the same proteins, i.e., the same phosphorylated tyrosines.

Yet further, attached as Exhibit C is a product insert for Zymed Laboratories PY-Plus Mouse anti-Phosphotyrosine (Cocktail) product. Under the heading "Reactivity" the product insert reads, "[i]t is well established that no one monoclonal antibody can react with all tyrosine phosphorylated proteins."

In view of such evidence, it can not be assumed or even expected that antibodies reported by Buday and Hirth would "specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4."

Indeed, the Federal Circuit has made clear that rejection can not be sustained on such basis. Thus, in *Continental Can Co. USA, Inc. v. Monsanto Co.*, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991), the Federal Circuit stated (bold emphasis added):

> Inherency, however, may not be established by probabilities or possibilities. **The mere fact that a certain thing may result from a given set of circumstances is not sufficient.**

In view thereof, reconsideration and withdrawal of the rejection are earnestly solicited.

Claims 123 and 132-142 were rejected under 35 U.S.C. § 103(a) over Buday in further view of Queen et al. (US Patent No. 6,180,3170). The rejection is respectfully traversed.

As discussed above, Buday does not necessarily at all teach a purified antibody which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4. Queen et al. does not cure the deficiencies of Buday and therefore the combination of Buday and Queen et al does not render claims 123 and 132-142 obvious. Nowhere does Queen teach a humanized antibody generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4. Accordingly, Applicants request the withdrawal of the rejection and allowance of the claims.

Claims 122, 130, 138, and 142 are rejected under 35 U.S.C. § 112, second paragraph on grounds of indefiniteness. The rejections are respectfully traversed.

Claims 122 and 142 were rejected for reciting "fully humanized." Claims 122 and 142 have been canceled without prejudice merely to expedite prosecution. Claims 130 and 138 were rejected for reciting "a 40 kd protein" and then referring again to the "40 kd protein" later in the claim. Applicants believe it is clear that the phrase "the 40 kd protein" refers back and has

antecedent basis from "a 40 kd protein." Applicants confirm that they are indeed the same protein. Withdrawal of the rejections are requested.

Claims 103-122 were rejected under 35 U.S.C. § 112, first paragraph. The rejections are respectfully traversed.

Support for the phrase "generated against a polypeptide comprising at least five non-phosphorylated amino acids," may be found in several places in the specification. For example, the phrase is supported at least by the following excepts from the specification:

> "ix). Generate panels of anti-LAT antibodies- antibodies that bind phosphorylated and **non-phosphorylated regions of LAT**."
> (Page 54, lines 22-23).

> "Both polyclonal and monoclonal antibodies are obtainable by immunization with LAT, **LAT fragments**...."
> (Page 38, lines 15-16).

> "LAT fragments ... are at least 5, usually at least 6, more usually at least about 8, most usually at least about 10 amino acids."
> (Page 44, lines 6-8).

> "LAT , one of the most prominently tyrosine phosphorylated protein[s] following TCR engagement has been identified. Deduced amino acid sequence identifies a novel integral membrane protein containing **multiple potential tyrosine phosphorylation sites.**"
> (Page 36, lines 2-5).

"Maximum phosphorylation of LAT was seen after stimulation for 15 seconds, and after 2 minutes LAT was **rapidly dephosphorylated**."
(Page 67, lines 22-23).

Thus, the specification, as evidenced by these excepts, supports the phrase "generated against a polypeptide comprising at least five non-phosphorylated amino acids." As is seen above, not every tyrosine is phosphorylated at every moment because the phosphorylation state of the LAT protein is dynamic. Also as seen above, the specification teaches that antibodies can be made from LAT fragments and antibodies from non-phosphorylated regions of LAT are contemplated, which would include regions containing tyrosines because not all tyrosines are phosphorylated at all times. Withdrawal of the rejection is therefore requested.

It is believed the application is in conditions for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

Date: April 13, 2005

Stephana E. Patton (Reg. 50,373)
Peter F. Corless (Reg. 33,860)
EDWARDS & ANGELL, LLP
P.O. Box 55874
Boston, MA 02205
Telephone: 617-439-4444
Facsimile: 617-439-4170

Customer No.: 21874